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APPLICANTS: Chagnaud *et al.*
ASSIGNEE: Centre National de la Recherche Scientifique
SERIAL NUMBER: 09/331,980 EXAMINER: Phuong Huynh, Ph.D.
FILING DATE: November 26, 1999 ART UNIT: 1644
FOR: ANTIBODIES SPECIFICALLY RECOGNIZING A NITROSYLATED PROTEIN, THEIR
METHOD OF PREPARATION, THERAPEUTIC USE AND DIAGNOSIS

May 7, 2001
Boston, Massachusetts

Assistant Commissioner for Patents
Washington, D.C. 20231

RESPONSE TO REQUIREMENT FOR RESTRICTION

This paper is in response to the March 7, 2001 Restriction Requirement (Paper No. 7). A check in the amount of \$55.00 is enclosed to cover the petition fee for a one-month extension of time pursuant to 37 C.F.R. § 1.17(a)(1). With the extension, these documents are due on or before May 7, 2001. Please charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 19904-001).

REMARKS

Applicants provisionally elect the invention of Group I, (Claims 1-5, 11 and 14), drawn to a purified antibody that binds a nitrosylated protein and a pharmaceutical composition, with traverse. The Examiner stated that "[t]he inventions listed as Groups 1-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features." According to the Examiner, the invention of Group I has no special technical feature that defines the contribution over Ye *et al.* (Methods in Enzymology, 269: 201-209, 1996). The Examiner has alleged that "Ye *et al.* teaches how to make and use polyclonal and monoclonal antibodies that recognizes a [sic] **nitrosylated proteins** including albumin..." and concludes that "[s]ince Applicant's inventions do not contribute a special technical feature over the prior art, they do not have single general inventive concept and lack unity of invention."

Applicants respectfully traverse. Applicants disagree with the Examiner's characterization of the prior art reference. Ye *et al.* describes production of antibodies against **nitrated proteins** and not **nitrosylated proteins**, as asserted by the Examiner. A skilled artisan would understand that a "nitrated protein" contains NO₂ groups. The introduction of a such NO₂ groups is obtained by peroxynitrite oxidation. ELISA assays indicate that those specific antibodies effectively bind nitrated proteins and also that this binding is displaced by nitrotyrosine or other compounds having a NO₂ group in ELISA competition assays. In contrast, **the antibodies of the present application are not directed against nitrated proteins, but against nitrosylated proteins**, which are proteins having NO groups. The present application discloses the introduction of nitrosyl groups on cysteine residues of the carrier protein by nitrosylation of the thiol group by means of a NO donor, sodium nitrite.

Therefore, Ye *et al.* neither teaches antibodies raised against nitrosylated proteins nor the method to obtain them by use of a nitrosylated immunogen. Furthermore, Ye *et al.* does not teach the method to produce such nitrosylated immunogens by NO transfer with a NO donor such as sodium nitrite. Accordingly, Applicants respectfully submit that the present invention is drawn to methods and compositions based on the genus of nitrosylated protein, antibodies, immunogens and methods set forth in the claims. This generic nitrosylated protein set identified in the specification as originally filed arises from the single inventive concept of utilizing the nitrosylated proteins in various related ways. Applicants respectfully request reconsideration and withdrawal of the present Restriction Requirement.

CONCLUSION

In view of the arguments made herein, Applicants respectfully submit that the outstanding Restriction Requirement is improper and should be withdrawn. If the Examiner believes that a telephone conversation with Applicant's Attorney would be helpful in expediting prosecution of this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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